REMARKS/ARGUMENTS

With this amendment, claims 43-49 are pending. Claims 1-42 are cancelled. For convenience, the Examiner's rejections are addressed in the order presented in an April 18, 2006, Office Action.

I. Status of the claims

Claim 43 is amended to recite that the nucleic acid is amplified from a Campylobacter genome. Support for this amendment is found throughout the specification, for example, at page 28, lines 9-13; and at page 46, line 26 through page 47, line 5. This amendment adds no new matter.

II. Objections to the drawings

Figure 3 is objected to for alleged non-compliance with the sequence listing rules. In order to expedite prosecution, the legend of Figure 3 is amended to include SEQ ID NO's of the amino acid sequences depicted in Figure 3. In view of this amendment, withdrawal of the objection to the drawings is respectfully requested.

III. Information disclosure statement

The Office Action objects to the Information Disclosure Statement (IDS). In order to expedite prosecution, a supplemental IDS is submitted with this response.

IV. Objections to the specification

The Office Action objects to the presence of hyperlinks in the specification. In order to expedite prosecution, the specification is amended to remove hyperlinks.

The Office Action objects to a paragraph at page 57, alleging that Table 4 should include a designation of the enzyme cst-II, also referred to as ORF #7a, see, *e.g.*, Table 3. Applicants respectfully disagree. Table 4 discloses results of NMR to identify chemical linkages in the products synthesized using the cloned glycosyltransferases. The vertical heading (left

most column) indicates specific linkages of sugar residues in the product oligosaccharides, including, *e.g.*, αNeu5Ac(2,3) and αNeu5Ac(2,8). The αNeu5Ac(2,3) and αNeu5Ac(2,8) linkages are found in the products of the claimed sialyltransferases, as those of skill are aware. An identical table appeared in a peer reviewed journal, indicating that those of skill are aware of the expected linkages for products of sialyltransferase reactions. *See, e.g.*, Table I of Gilbert *et al.*, *J. Biol. Chem.* 275:3896-3906 (2000) at page 3899. Further explanation is not required.

V. Rejections for obviousness-type double patenting

Claims 43-49 are rejected for alleged obviousness-type double patenting over claims 1-5 of U.S. Patent No. 6,503,744 (the '744 patent). Applicants respectfully traverse the rejection. The nucleic acid claimed in the '744 patent is residues 350-1234 of SEQ ID NO:1, which encodes a lipid A biosynthesis acyltransferase and therefore does not have the sialyltransferase activity required by the pending claims. Applicants also submit as Exhibit D an alignment of the recited primers SEQ ID NO:46 and the reverse complement of SEQ ID NO:47 with the nucleic acid claimed in the '744 patent or with SEQ ID NO:2. The primers align with the 3' and 5' ends of SEQ ID NO:2. Similar results are obtained for, *e.g.*, SEQ ID NOs: 4, 6, 8, 11, and 13. In contrast, the primers align with the '744 nucleic acid only with inclusion of substantial gaps at almost the same portion of the '744 nucleic acid. Thus, the recited primers would not produce a PCR product using as a template the nucleic acid claimed in the '744 patent. Therefore, this rejection for alleged obviousness-type double patenting should be withdrawn.

Claims 43-49 are rejected as allegedly unpatentable under the judicial doctrine of obviousness type double patenting over claims 1-15 of U.S. Patent No. 6,669,705. In order to expedite prosecution of this application, Applicants submit a terminal disclaimer of the term of a patent granted on the instant application over U.S. Patent No. 6,669,705. Applicants note that the filing of a terminal disclaimer to obviate a rejection based on non-statutory double patenting is not an admission of the propriety of the rejection. See, MPEP §804.02. Accordingly, Applicants respectfully request withdrawal of the rejection.

Claims 43-49 are rejected for alleged obviousness type double patenting over claims 43-58 of co-pending US Application No. 10/734,719. Applicants will file terminal

disclaimers to overcome these rejections, if appropriate, when the claims are deemed otherwise allowable.

VI. Rejections under 35 U.S.C. §112, second paragraph

Claims 43-49, according to the Office Action, fail to particularly point out and distinctly claim the subject matter regarded by the Applicants to be the invention. In particular, the Office Action alleges that use of the term "amplified by PCR" renders the claim indefinite in the absence of conditions under which the PCR reaction is performed. Applicants respectfully traverse the rejection.

According to the Federal Circuit, "[35 U.S.C.] §112, second paragraph, requires a determination of whether those skilled in the art would understand what is claimed in light of the specification." *Orthokinetics v. Safety Travel Chairs Inc.*, 1 USPQ2d 1081 (Fed. Cir. 1986); *see also* MPEP 2173.02. In *Orthokinetics* the court ruled that a claim to a wheelchair designed to fit "between a doorframe of an auto and one seat" was not indefinite, even though measurements varied based on the particular automobile. The court recognized that those of skill could easily measure the distance required by any particular automobile. The court also stated that patent law did not require listing all possible lengths corresponding to dimensions of hundreds of automobiles in the specification, much less the claims. Moreover, if the claims reasonably inform those of skill of the utilization and scope of the invention and the language is as precise as the subject matter permits, the requirement of §112, second paragraph are satisfied. MPEP §2173.05(a) and *Hybritech Inc. v. Monoclonal Antibodies, Inc.* 231 USPQ 81, 94 (Fed. Cir. 1986). In *Hybritech*, a claim that recited a value for the affinity of an antibody was found to be definite, because, even though the assay for measurement was not standard, determination of antibody affinity was known at the time of filing. Applicants assert that one of ordinary skill in the art would understand the claimed invention in light of the specification and that the phrase "amplified by PCR" is sufficiently precise to define the claimed nucleotide sequences.

First, PCR was an extremely well-known and widely used method at the time of filing. In the specification, the PCR conditions are described as those of the manufacturer. *See, e.g.*, specification at page 47, lines 4-6. The specific PCR primers used are also disclosed in the

specification. *See, e.g.*, specification at page 48, lines 10-11 and Table 2. Second, the specification discloses that PCR reactions performed using the specific primers under the manufacturer's recommended conditions resulted in PCR products that encoded an active sialyltransferase protein. Third, Applicants have amended the claims to reflect that the template for PCR is a *Campylobacter* genome.

Applicants present three references as evidence that PCR methodology was well known and understood by those of skill at the time of filing: Saiki, The Design and Optimization of the PCR, pages 7-16 in PCR Technology: Principles and Applications for DNA Amplification, 7-16 (Erlich ed., 1992, Exhibit A); Stryer *et al.*, Biochemistry, 132-134 (1995, Exhibit B); and Pwo DNA Polymerase, Roche Applied Science, (2006, Exhibit C). Roche acquired Boehringer Mannheim, original manufacturer of Pwo polymerase.

Saiki discloses the "standard PCR reaction" at page 8. Saiki also discloses that the standard reaction is adequate for most PCR, and if not provides a starting point for optimization of the reaction. *See, e.g.*, Saiki at pages 8 and 16. Saiki also provides extensive discussion of how and which parameters to vary when optimizing a PCR reaction. *See, e.g.*, Saiki at pages 8-15. Saiki also discloses at page 8, that the most crucial variable for any PCR reaction is the choice of primers. Thus, Applicants recite the most crucial variable for successful PCR in the claims.

Stryer is an undergraduate biochemistry text and also discloses standard conditions for PCR reactions at page 133. Stryer also points out that PCR amplification is very specific, because of the stringency of primer hybridization to template at high temperature. Like the other references, Stryer discloses an annealing temperature between 50° and 55° C.

Applicants also submit the manufacturer's specification included with PWO polymerase. The PWO polymerase specification discloses standard PCR conditions for the PWO polymerase, as well as suggested protocols for modification if necessary.

In summary, the submitted references show that the standard conditions for PCR and protocols to optimize the reaction were very well-known at the time of filing. A listing of the thousands of different reaction conditions that could possibly be used for amplification is not required in specification or in the claims. The submitted references also demonstrate that the

primer sequence is most critical for successful PCR amplification. As Applicants provide the primer sequences in the claims, the claims would be understood by those of skill and are thus, not indefinite.

In view of the above amendments and remarks, withdrawal of the rejection under 35 U.S.C. §112, second paragraph is respectfully requested.

VII. Rejections under 35 U.S.C. §112, first paragraph, enablement

Claims 43, 44, and 46 are rejected for allegedly failing to provide enablement for those of skill to make and use the invention in a manner corresponding to the scope of the claims. To the extent the rejection applies to the amended claims, Applicants respectfully traverse the rejection.

Factors such as the amount of guidance presented in the specification and the presence of working examples must be considered to determine whether undue experimentation is required to practice the claimed invention (*see*, *Ex Parte Forman*, 230 USPQ 546 (Bd. Pat. App. & Int. 1985) and *In re Wands*, 8 USPQ2d 1400 (Fed. Cir. 1988)). As described in *Wands*, "a considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed" (*see*, *Wands*, USPQ2d at 1404, quoting *In re Jackson*, 217 USPQ 804 (Bd. Pat. App. & Int. 1982)). Moreover, "[a] patent need not teach, and preferably omits, what is well known in the art." MPEP 2164.01 *citing In re Buchner*, 18 USPQ2d 1331, 1332 (Fed. Cir. 1991); *Hybritech, Inc. v. Monoclonal Antibodies, Inc.*, 231 USPQ 81, 94 (Fed. Cir. 1986), *cert. denied*, 480 U.S. 947 (1987); *Lindemann Maschinenfabrik GMBH v. American Hoist & Derrick Co.*, 221 USPQ 481, 489 (Fed. Cir. 1984).

As set forth in the Manual of Patent Examining Procedure (MPEP) § 2164.01, "the test of enablement is not whether any experimentation is necessary, but whether... it is undue." Further, the "fact that experimentation may be complex does not necessarily make it undue, if the art typically engages in such experimentation" (citations omitted). Finally, claims reading on inoperative embodiments are enabled if the skilled artisan understands how to avoid

inoperative embodiments. *See, e.g., In re Cook and Merigold*, 169 USPQ 299, 301 (C.C.P.A. 1971).

The claims are now directed to a nucleic acid molecule that can be PCR amplified from a *Campylobacter* genome and that encodes a polypeptide with α-2,3-sialyltransferase activity. The claims provide specific primers that are used for PCR amplification of the claimed nucleic acids. PCR is a well-known and standardized molecular biology technique. Moreover, optimization of PCR conditions, if needed, is entirely routine to those of skill. Further, the most critical factor in the success of a PCR reaction is the choice of primers and specific primers are recited in the claims. If the claims read on inoperative embodiments of the claims, those of skill can easily distinguish between operative and inoperative embodiments using the disclosure of the specification and knowledge in the field at the time of filing.

The Office Action states that the claims enable the polynucleotide of SEQ ID NO:2, but alleges that other polynucleotides that encode sialyltransferase proteins are not enabled. Applicants assert that the other polynucleotides that encode sialyltransferase proteins and that are amplified from a *Campylobacter* genome using primers comprising SEQ ID NO:46 and 47 are disclosed in the specification and, thus, are enabled. For example, SEQ ID NO's:4, 6, 8, 11, and 13 each encode a polypeptide with α-2,3-sialyltransferase activity and can be amplified from a *Campylobacter* genome using primers comprising SEQ ID NO:46 and 47. A representative alignment of SEQ ID NO:2 with primers SEQ ID NO:46 and 47 is found in Exhibit D.

Applicants also assert that, with standard PCR conditions as described above, the PCR reaction using primers comprising SEQ ID NO:46 and 47 is a very specific reaction. Of the *Campylobacter* sialyltransferases disclosed in the application, SEQ ID NO's:2, 4, 6, 8, 11, and 13 can be amplified from a *Campylobacter* genome using primers comprising SEQ ID NO:46 and 47 using standard PCR conditions. However, two of the disclosed *Campylobacter* sialyltransferases, SEQ ID NOs:10 and 48, are encoded by nucleic acids that cannot be amplified using primers comprising SEQ ID NO:46 and 47 using standard PCR conditions. Thus, those of skill can make and use the claimed nucleic acids and can distinguish operative from inoperative embodiments. Applicants respectfully remind the Examiner that any polypeptide that is encoded

by the claimed nucleic acids can be assayed for the recited sialyltransferase activity using assays disclosed in the specification.

The Office Action alleges that the choices of PCR conditions are essentially infinite. The Office Action cites Kramer and Coen (2001) as supporting the unpredictability of obtaining a product suing PCR amplification techniques. This is incorrect because, as discussed above, standard PCR conditions and methods to optimize those conditions were well known at the time of filing. Moreover, Kramer and Coen disclose standard techniques to modify PCR standard conditions, as do the references discussed above. Kramer and Coen also disclose that generation of PCR primers is the least predictable factor in PCR and the most difficult to troubleshoot. *See, e.g.*, Unit 15.1.7. The specific primers used to produce the claimed nucleic acids are recited in the claims. Kramer and Coen discuss the use of a variety of thermostable polymerases, including Pwo polymerase. *See, e.g.*, Table 15.1.4. Kramer and Coen also direct those of skill to commercially available kits that can be used to easily and routinely optimize PCR conditions. *See, e.g.*, Table 15.1.3.

Kramer and Coen begin their discussion of PCR at Unit 15.1 by stating the following: "This unit describes a method of amplifying DNA enzymatically by the polymerase chain reaction (PCR), including procedures to quickly determine conditions for successful amplification of the sequence and primer sets of interest and to optimize for specificity, sensitivity, and yield." Thus, Kramer and Coen describe the disclosed PCR procedures as "quickly" performed by those of skill. Moreover, the optimization methods disclosed by Sakai in 1992 do not differ substantially from the optimization methods disclosed by Kramer and Coen in 2001. As the optimization methods were apparently used by those of skill for at least nine years without significant modification, the methods are appropriately described as routine. Any modification specific to use of a different polymerase, *e.g.*, Pwo polymerase, is taught by the manufacturer, and not left for those of skill to determine. Thus, the methods used to make the claimed nucleic acids are enabled.

In order to establish a prima facie case of lack of enablement, the Examiner has the burden to establish a reasonable basis to question the enablement provided for the claimed invention. *In re Wright*, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993). The Examiner has not

provided any reason why those of skill would not be able to PCR amplify the claimed nucleic acids from a *Campylobacter* genome using the recited primers and methods well-known to those of skill. Applicants respectfully assert that based on the recitation of specific primers in the claims, the disclosure of sialyltransferase assays in the specification, and the widespread knowledge of PCR techniques at the time of filing, the claimed nucleic acids are enabled.

In view of the above amendments and remarks, withdrawal of the rejection for alleged lack of enablement is respectfully requested.

VIII. Rejections under 35 U.S.C. §112, first paragraph, written description

Claims 43, 44 and 46-49 are rejected for allegedly containing subject matter that was not described in the specification in a manner to convey that the inventors had possession of the invention at the time of filing the application. According to the Office Action, the specification teaches the structure of only a single representative species of the claimed genus and fails to described any other representative species with other than functional characteristics. Thus, the Office Action appears to allege that Applicants have not identified a representative number of species from the claimed genus. To the extent the rejection applies to the amended claims, Applicants respectfully traverse.

According to the MPEP, the written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant, identifying characteristics, *i.e.*, structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus. MPEP §2163, *citing University of California v. Eli Lilly & Co.*, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997).

The specification provides description of a representative number of the claimed nucleic acids through both reduction to practice and disclosure of relevant identifying characteristics. For example, SEQ ID NO's:2, 4, 6, 8, 11, and 13 each encode a polypeptide with α-2,3-sialyltransferase activity and can be amplified from a *Campylobacter* genome using

primers comprising SEQ ID NO:46 and 47. The relevant identifying characteristics are both structural, *e.g.*, the specific primers that can be used to amplify the claimed nucleic acids from a *Campylobacter* genome and functional, *e.g.*, the enzymatic activity of the encoded 2,3-sialyltransferase proteins. The specification, therefore, exemplifies a representative number of species from the claimed genus and thus provides notice to those of skill that the inventors had possession of the claimed invention at the time of filing.

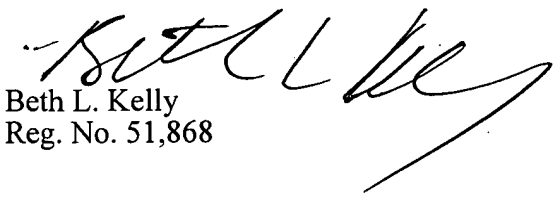
In view of the above amendments and remarks, withdrawal of the rejection for alleged lack of written description is respectfully requested.

CONCLUSION

In view of the foregoing, Applicants believe all claims now pending in this Application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 415-576-0200.

Respectfully submitted,



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